Prevalence of Rheumatoid Arthritis and DMARDs Usage in Indian Population: A Cross-Sectional Study

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Abstract

Background: Rheumatoid arthritis (RA) is an autoimmune disorder characterized by symmetric and erosive synovitis with extra-articular involvement in some cases. RA prevalence in India is 0.75%. The study is to estimate the prevalence of RA in the South Indian population and to determine the demographic characteristics such as gender, age, geographical locality, and usage of antirheumatic drugs. **Methodology:** This prospective cross-sectional study was conducted in 600 patients of both male and female at advance rheumatology center. The patients were selected based on inclusion and exclusion criteria. Patients who are suspected and diagnosed newly with RA, patients who are already with RA attending the rheumatoid center and are on therapy, and patients age equal to and above 16 years either gender are included in the study. Patients with other arthritic and immunologic problems such as osteoarthritis, psoriatic arthritis, systemic lupus erythematosus, spondylosis, and osteoporosis were excluded from the study and patient's age below 16 years are excluded from the study. **Results:** Among 600 patients presented to advance rheumatology center, 174 patients are identified with classical symptoms of RA, in those female and male patients are 132 and 42, respectively. The mean age of total patients is 45.51 ± 12.09. The estimated prevalence was found to be 0.29 or 29% (95% confidence interval is 0.25–0.33). Disease-modifying antirheumatic drugs (36.9%) are mostly prescribed. **Conclusion:** This study witnessed a rise in the prevalence of RA in South Indian population which gives alarming signals to the health authority and policymakers to increase the awareness on RA in India.

Key words: Disease-modifying antirheumatic drugs, prevalence, rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is defined as a chronic systemic inflammatory disorder characterized by symmetrical polyarthritis deforming of varying extent and severity, associated with synovitis of joints, tendons sheaths, articular cartilage loss, and erosion of juxta-articular bone.[1] Normally, the immune system can differentiate between self and non-self. In RA, white blood cells view the synovium (tissue that nourishes cartilage and bone) as non-self and initiate an inflammatory attack.[2] The worldwide prevalence of RA in overall population is 0.8% approximately; among them, adults are 0.5–1% approximately. The prevalence of RA in women was 3 times more when compared to men.[3,4] The declining incidence with the lack of improvement in survival of patients with RA resulted in the reported decrease in the prevalence of RA. The recent studies revealed that the incidence was 54/100,000 in women and 24.5/100,000 in men.[3] In developed countries like the UK, the prevalence of RA is 1.16% in women and 0.44% in men, and in the US and Europe, it is 0.8 and 1.1%, respectively, while in Native Americans, it is 6.8%.[1,3] The prevalence is high in Pima Indians where it is low in Afro-Americans and Chinese that is 1–1.5%, the prevalence of RA is seen

in Caucasians with female-to-male ratio 3:1.[5] According to the World Health Organization data, the prevalence of RA varies between 0.3% and 1% and is more common in women and also in developed countries. The World Health Organization forecasted that at least 50% of patients in developed countries are unable to hold down a full-time job in next 10 years. In developing countries, the epidemiological studies show lower prevalence of RA when compared with Caucasians.[6] The median prevalence estimates of RA are 3.5 (range 2.4– 3.6).[7] The prevalence of RA in South and North Pakistan is estimated as 0.142 and 0.55%, respectively.[7] The prevalence of RA in males in low- and middle-income countries is 0.16% and 0.75% in females.[8] RA prevalence in India is 0.75% which is slightly similar that is 0.8% in Manchester.[9]

Rising of RA can be seen by the following factors: Age, gender, genetic factors, infectious agents, lifestyle, and hormonal factors. Among these factors, some may increase the risk of RA and others are protective role in disease development. Risk of RA is 3 times more in men who smoke. Hormonal disturbances may play an important role in promoting RA in women.[3] The drugs most frequently used in initial therapy are the DMARDs and the nonsteroidal anti-inflammatory drugs (NSAIDs). Unlike the NSAIDs, which reduce the symptoms but not the progress of the disease, the former group may halt or reverse the underlying disease itself.[10] In the past few decades, essential improvements in the treatment of RA and other auto-inflammatory diseases have been made by the introduction of biologic disease-modifying antirheumatic drugs (b-DMARDs).[11] Recently, a significant increase in any DMARDs use in RA patients was observed in North America, Germany, and the United Kingdom.[12] Although there is still no known cure for RA, treatment with non-bDMARDs and/or bDAMRDs is considered as the standard of care for RA.[13]

There are relatively a few studies are available on epidemiology of RA and these studies are majorly performed in North India. Due to the genetic and lifestyle variability from North India to the South Indian people, the researchers attempted to perform the same in the South Indian population.

METHODOLOGY

Study design and setting

This study, prospective cross sectional in nature was carried out at advance rheumatology center, Kurnool, during the period from December 2015 to May 2016. The Institutional Review Board approval was taken before the conductance of the study (CESCOP/IEC/PHRD/001). A total of 600 patient's data were collected from male and female individuals. The study begins with the selection of the patients based on the inclusion criteria followed by the collection of all the baseline parameters of the patients demographic details, medical history, past allergies, personal history, family

history, laboratory data, and present treatment and all the data of the subjects are collected using the standard patient data pro forma. The inclusion and exclusion criterion of the study includes:

Inclusion criteria

- Patients who are suspected and diagnosed newly with RA.
- Patients who are already with RA attending the rheumatoid center and are on therapy.
- Patients age equal to and above 16 years.
- Either gender is considered.
- Patients who are coming for regular follow-ups.

Exclusion criteria

- Patients with other arthritic and immunologic problems such as osteoarthritis, psoriatic arthritis, systemic lupus erythematosus, spondylosis, and osteoporosis are excluded from the study.
- Patients age below 16 years.
- Juvenile arthritis was excluded.

Statistical analysis

The statistical analysis was carried out for prevalence which was estimated using 95% confidence interval in Excel and the mean± standard deviation were used for age.

RESULTS

Demographic data

A total of 600 patients are presented to the advance rheumatology center, in which 174 (29%) patients are identified with classical symptoms of RA (Table 1 shows demographic distribution of RA patients among tested attributes). Among $n = 174$, the highest patients with RA are 58 (33.3%) and are placed under the age frequency of 45–54 with an overall mean age of 45.51 ± 12.09. Out of 174 RA patients, the gender distribution is as follows, that is, females are 132 (75.9%) and males are 42 (24.13%), the female-to-male ratio shows 3:1. The frequency of age distribution shows similar in both genders which is 45–54 years of age and is screened to be highly effected with RA, that is, $n = 44$ (33.3%) in females and $n = 14$ (33.4%) in males.

The distribution based on locality is categorized into urban, semi-urban, and rural regions. Patients under urban region are more, that is, 101 (58%), whereas patients under semi-urban and rural region are 36 (20.9%) and 37 (21.1%), respectively. The highly screened patients with RA seen in urban locality and are females with 80 (45.9%).

Medical history

In these 174 RA presented to the advance rheumatology center, 64 (41%) of cases are identified with past diagnosis of RA, in which 41 patients are with only RA and others 23 patients are with RA and other diseases. The other diseases include thyroid diseases, hypertension, diabetes mellitus, coronary artery disease, chikungunya, asthma, seizures, and systemic lupus erythematous as shown below. In our study, the highest diagnosis, that is, four diseases is seen in only one patient and lowest diagnosis, that is, one disease in 122 patients [Figure 1].

Table 1: Demographic data

Demographics	Total	Mean
Age distribution		
16–24	9 (5.2%)	45.51±12.09
25–34	21 (12.5%)	
35–44	46 (26.4%)	
45–54	58 (33.3%)	
55–64	30 (17.2%)	
>65	10 (5.7%)	
Gender distribution		
Male	42 (24.1%)	-
Female	132 (75.9%)	
Personal habits		
Smoking	4 (2.2%)	-
Alcoholic	5 (2.8%)	
Family history	10 (5.7%)	
Geographical localities		
Urban	101 (58%)	-
Semi-urban	36 (20.9%)	
Rural	37 (21.1%)	

Erythrocyte sedimentation rate (ESR)

Among 174 patients, ESR is carried out in 90 (51.72%), of which 30 (33.4%) of patients show the ESR value at the range between 51 and 100 mm/h. The highest value of ESR 150 mm/hr is found in one patient in our study [Table 2].

Laboratory parameters in RA

The elevated C-reactive proteins (CRPs) show the heightened disease stage in RA diagnosed patients. Out of 174 patients, CRP was done in 60 (34.5%), RA factor in 111 (63.8%), and anti-cyclic citrullinated peptide in 12 (6.9%) [Figure 2].

Most prescribed drugs

In general, prescribed drugs in RA are DMARDs, NSAIDs, folic acid supplements, gastrointestinal agents, and other calcium and vitamin supplements. In our study, the most prevalent drugs prescribed are DMARDs, NSAIDs, calcium supplements, proton-pump inhibitors, chondroitin, multivitamin, ranitidine, and others, as shown in Table 3.

When categorized among these DMARDs, the mostly prescribed drugs are in the order prednisolone > hydroxychloroquine > methotrexate > sulfasalazine > leflunomide > azathioprine > golimumab > infliximab > dexamethasone and are shown in Table 4.

DISCUSSION

Our cross-sectional study was conducted in 600 patients out of which 174 patients are diagnosed with RA the estimated prevalence was found to be 0.29 or 29% (95%, confidence
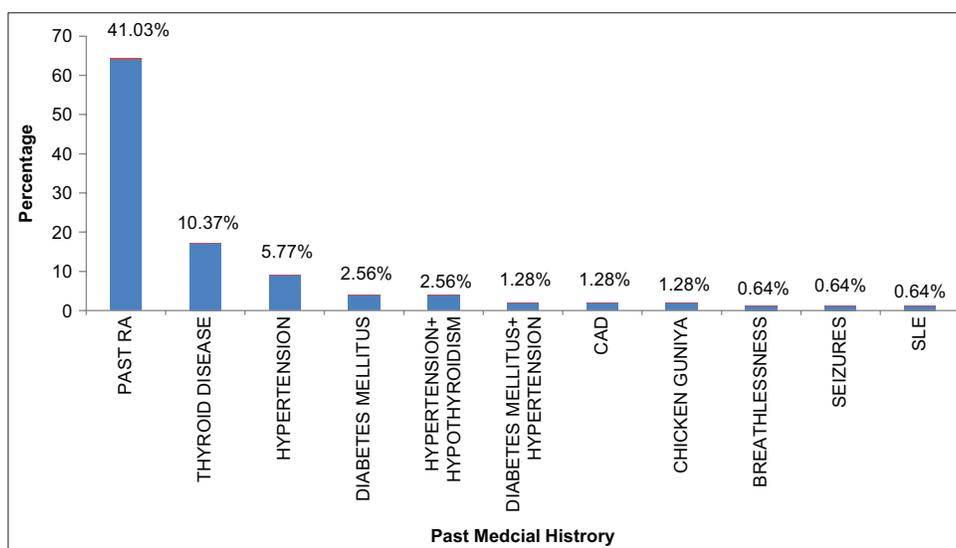
Figure 1: Distribution of patients based on medical history. CAD: Coronary artery disease, SLE: Systemic lupus erythematosus

interval [CI] is 0.17–0.19) and Carmona *et al*. The estimated prevalence was 0.5% (95%, CI is 0.25–0.85).

The female-to-male ratio was 3:1 comparative with Chopra *et al*. and Malaviya *et al*. who described female-to-male ratio 3:2 and 9:1, respectively, and also stated that this difference in prevalence of RA in female may be due to postmenopausal stages with estrogen imbalance in female patients.[14,15]

The prevalence of RA in our study is more in the age group of 45–54 years and the mean age of onset was 45.51 ± 12.09. In this female age group of 45–54 years with a mean onset of 45.51 ± 12.13 and male age group of 45–54 years with a mean onset of 46.38 ± 12.46 seen more occurrence of Rheumatoid arthritis. Our results are similar when compared with the results of Chopra *et al*. with the age frequency of 45–54 years.

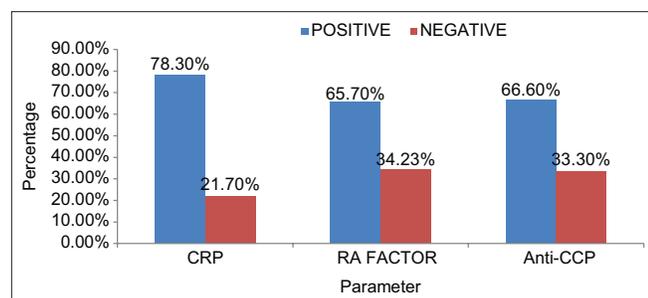In the present study, we found that RA was more in urban people 58% compared to the semi-urban 20.9% and rural 21.1% of people. This is because of the study was mainly done in the district levels advance rheumatology center.

The comorbidities found in our study thyroid disease 10.5% followed by hypertension 5.6% and hypertension with hypothyroidism 2.6%. In our study, the occurrence of thyroid disease with RA is found with higher percentage 13%, it was assumed that in RA patients, genetic predisposition occurred due to auto immunity in patients with thyroid, whereas when compared with Alam *et al*. study, the hypertension was predominant comorbidity occurred with 13.74%.[8]

Table 2: Range of ESR level

ESR levels	Number of patients
<20	28 (31.1%)
21–50	25 (27.8%)
51–100	30 (33.3%)
101–150	7 (7.8%)

ESR: Erythrocyte sedimentation rate

Table 3: Most prescribed drugs

Drugs	Number of drugs prescribed	Percentage
DMARDs	361	36.9
NSAIDs	132	13.5
Calcium supplements	110	11.2
Folic acid	65	6.6
Chondroitin	66	6.7
Proton-pump inhibitor	99	10.1
Ranitidine	23	2.3
Multivitamin	35	3.6
Others drugs	88	9

DMARDs: Disease-modifying antirheumatic drugs, NSAIDs: Nonsteroidal anti-inflammatory drugs

Figure 2: Laboratory parameters in rheumatoid arthritis. CRP: C-reactive protein, anti-CCP: Anticyclic citrullinated peptide

Table 4: Most prevalent drugs prescribed in DMARD, NSAID, and others

Drugs prescribed	Number of drugs	Percentage
DMARDs		
Prednisolone	138	38.2
HCQS	133	36.1
Methotrexate	62	17.2
Sulfasalazine	11	3
Leflunomide	9	2.5
Azathioprine	4	1.1
Golimumab	2	0.5
Infliximab	1	0.3
Dexamethasone	1	0.3
Total DMARD	361	36.9
NSAIDs		
Aceclofenac+Paracetamol	105	79.5
Paracetamol	9	6.8
Aceclofenac	7	5.3
Naproxen	4	3
Celecoxib	4	3
Tramadol+Paracetamol	2	1.5
Naproxen+Paracetamol	1	0.7
Paracetamol+Ibuprofen	1	0.7
Total NSAID	132	13.5
Others		
Calcium supplements	110	11.2
Folic acid	65	6.6
Chondroitin	66	6.7
Rabeprazole	88	9
Pantoprazole	11	1.1
Ranitidine	23	2.3
Multivitamin	35	3.6
Others	88	8.9

DMARDs: Disease-modifying antirheumatic drugs, NSAID: Nonsteroidal anti-inflammatory drug

Among all patients with RA, rheumatoid factor was performed in 111 patients. The rheumatoid factor is positive in 65.8% among this female and male percentage is found to be 49.5% and 16.3%, respectively. This is quiet lower when compared with Alam *et al.* study reveals out of 4900 patients, rheumatoid factor was done in 633 patients with 74.4% positive and Malaviya *et al.* study out of 3393 patients, the rheumatoid factor was done in 219 patients with 82.2% positive.[8,14]

In our study, disease-modifying antirheumatic drugs are prescribed to 36.1% of patients. In DMARD category, the most commonly prescribed drugs are prednisolone (38.4%), hydroxychloroquine (36.3%), and methotrexate (17.3%), and in NSAID category, combination of aceclofenac and paracetamol (79.5%) is most commonly prescribed combination for pain relief, whereas in a study by Bhatt *et al.*, the most commonly prescribed drugs are ibuprofen and combinations.[16] In other category drugs, calcium supplements 11.23% are mostly prescribed.

The use of hydroxychloroquine is prescribed more that is 36.3% followed by prednisolone when compared with the study Rao *et al.* and Vardhan *et al.* The use of methotrexate and sulfasalazine among all DMARDs is predominant.[17,18] The use of biological DMARDs is very less which is only given in three patients as these agents are very expensive.

CONCLUSION

There were limited data available on the epidemiology of RA in South Indian population. The study brings attention on RA in South Indian population which gives alarming signals to the health authority and policymakers to increase the awareness on RA in India.

The prevalence of RA was increasing day by day in Indian population, so the government has to increase survey at urban and rural levels.

ACKNOWLEDGMENT

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